Slides for public observers-contains no ACIC

NICE National Institute for Health and Care Excellence

Ertugliflozin in triple therapy for treating type 2 diabetes

Lead Team presentation

1st appraisal committee meeting
Network meta-analysis and cost effectiveness
Committee A
Lead team: Graham Ash and Olivia Wu
ERG:University of Warwick Medical School
NICE technical team: Sana Khan, Zoe Charles
Company: MSD
8 January 2019

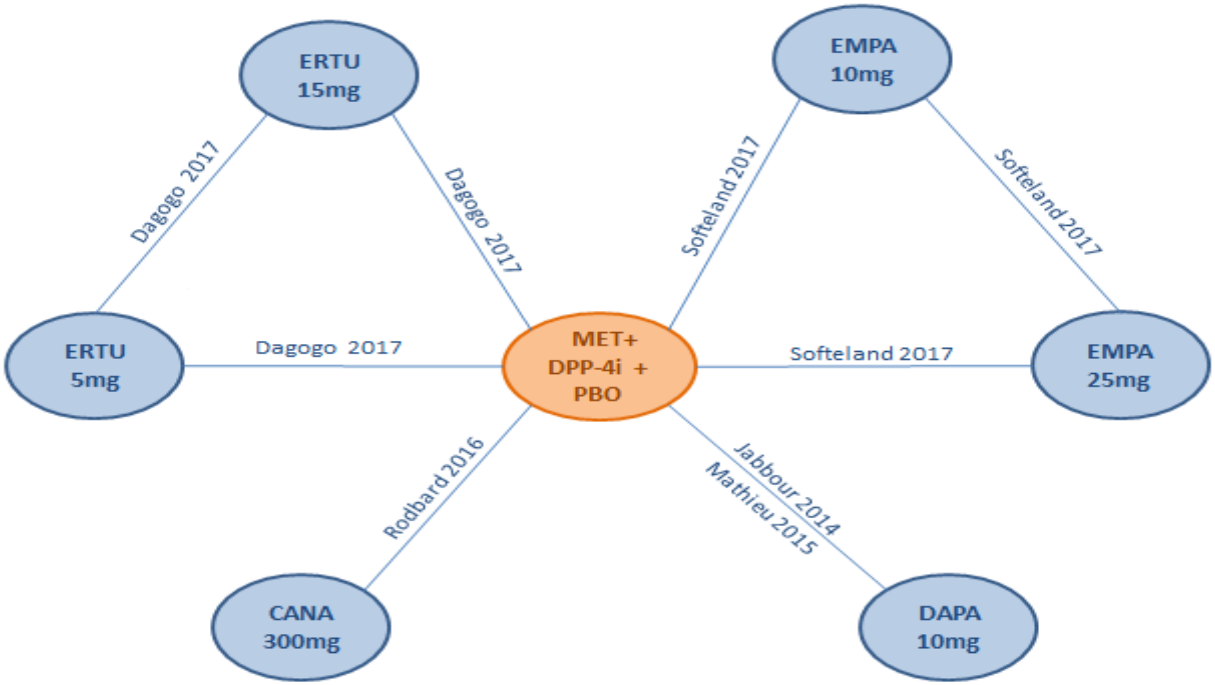
Key issues

- There is no direct evidence comparing ERTU with other flozins and the company conducted an indirect comparison. Does the committee accept the company's conclusions that ERTU has similar clinical effectiveness and safety to other flozins in the proposed triple therapy regimen?
- Does the committee accept the company's cost-minimisation approach based on the assumption that flozins have similar clinical effectiveness and safety and only differ in terms of drug acquisition costs?
- The ERG highlights that the triple therapy regimen proposed by the company costs more than some other triple therapy regimens used in clinical practice. What is the committee's view of the cost relative to other triple therapy combinations?

[redacted]

Company's network meta-analysis (NMA)

- Compared ERTU with other flozins on a background of metformin and a gliptin
- No other comparators in scope were included - company believes the only relevant comparators are other flozins with the same background therapies
- Included 5 RCTs (VERTIS SITA 2 (Dagogo 2018 - ERTU); Jabbour 2014 (DAPA); Mathieu 2015 (DAPA); Rodbard 2016 (CANA); Softeland 2017 (EMPA)
- Outcomes: **continuous**: change in HbA1c, weight and SBP. **Binary**: HbA1c in target; UTIs; genital mycotic infections. All measured at week 24 to 26



Company's NMA results

Continuous outcomes

- Change in HbA1c: ERTU 5 and 15 mg were statistically superior to DAPA 10mg (if using Jabbour 2014 but no differences if using Mathieu 2015)
- Weight change:
  [redacted]
- Change in SBP: no statistically significant differences between flozins

Binary outcomes

- HbA1c at target (<7.0%): no statistically significant differences between flozins
- All AEs / UTIs: no statistically significant differences between flozins

Company's conclusion

- ERTU has similar efficacy and safety in triple therapy to other flozins

[redacted]

ERG critique: company NMA

- Included trials were of good quality and broadly similar
- 3 different gliptins (sitagliptin, saxagliptin and linagliptin) were used in studies included in the NMA. The efficacy of these was assumed to be equal to allow a broader connected network. ERG agrees that this assumption is reasonable
- Although absolute equivalence is not proven, the company's NMA shows no clinically significant differences in glucose-lowering efficacy amongst the flozins:
  - effect on HbA1c of DAPA in the Jabbour 2014 trial at 26 weeks was smaller than in other DAPA trial but by 52 weeks the effect had increased to close to that of ERTU
- Instead of an NMA, ERG considers a simpler comparison of clinical effectiveness could have been carried out against just one flozin approved by NICE:
  - ERG compared VERTIS SITA 2 with the trial by Mathieu and colleagues of DAPA in combination with sitagliptin and metformin and concluded that this comparison provides reasonable evidence that ERTU is at least as effective as DAPA

Company's economic analysis

- Company considered cost minimisation to be the most appropriate form of economic analysis because the results of the NMA showed that all flozins have similar health benefits
- Only drug acquisition costs were considered in the cost minimisation analysis as there are no differences in testing, initiation, administration or monitoring costs between flozins
- 1 year time horizon was considered sufficiently long to capture any differences between the treatments

[redacted]

Drug acquisition costs

Therapy	Price per pack	Price per tablet	Dose per tablet	Daily dose	Annual cost
Background therapy					
Metformin	£0.90 per 28 pack	£0.03	500mg	2000 mg	£43.83
Gliptin (sitagliptin)	£33.26 per 28 pack	£1.19	100mg	100 mg	£434.65
Intervention					
ERTU	£[redacted] per 28 pack	£[redacted]	5 mg or 15 mg	5 mg or 15 mg	£[redacted]
Comparators					
CANA	£39.20 per 30 pack	£1.31	100 mg or 300mg	100 mg or 300mg	£478.48
DAPA	£36.59 per 28 pack	£1.31	10 mg	10 mg	£478.48
EMPA	£36.59 per 28 pack	£1.31	10 mg or 25 mg	10 mg or 25 mg	£478.48
Combination					
Met + gliptin + ERTU		£[redacted]			£[redacted]
Met + gliptin + CANA		£2.53			£956.96
Met + gliptin + DAPA		£2.53			£956.96
Met + gliptin + EMPA		£2.53			£956.96

[redacted]

Base-case results

Technologies	Total costs	Total LYG	Total QALYs	Incremental costs vs. ERTU
Metformin + gliptin + ERTU 5 mg /15 mg	£[redacted]	-	-	
Metformin + gliptin + CANA100 mg /300 mg	£956.96	-	-	[redacted]
Metformin + gliptin + DAPA 5 mg /10 mg	£956.96	-	-	[redacted]
Metformin + gliptin + EMPA 10 mg /25 mg	**£956.96**	-	-	[redacted]

- CANA, DAPA and EMPA all have an annual cost of £478.48 (£1.31 per day * 365.25 days)
- ERTU [redacted] with an annual cost of [redacted] per day * 365.25 days),

[redacted]

[redacted]

ERG critique of company's cost-minimisation analysis

- Company's justification of a cost-minimisation approach on the basis of NMA results showing similar efficacy and safety is valid
- Assumptions of cost minimisation analysis are reasonable (no differences in administration/monitoring costs of flozins and 1 year time horizon)
- ERG agrees that ERTU results in an [redacted]
- Company's case, based on prescribing data, is that the triple therapy regimen of a flozin + metformin + gliptin is sufficiently used in UK for it to be considered standard therapy. However, it is relatively expensive compared with other triple therapy regimens
  - could be argued that company's proposed regimen is appropriate only when patients cannot take either sulfonylureas (SU) or pioglitazone (PIO)

Combination	Annual cost
Metformin + SU + PIO	£76
Metformin + gliclazide* MR + PIO	£108
Metformin + SU + gliptin	£479
Metformin + gliclazide + flozin	£568
Metformin + gliptin+ PIO	**£471**
Metformin + gliptin+ flozin (CANA, DAPA or EMPA)	**£927**

*Based on past appraisals gliclazide is ERG's preferred SU based on efficacy and AEs

[redacted]

Equalities issues

- No equality issues have been raised by the company or patient and professional groups

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